61. (Amended) The kit of claim 36, wherein the DNA of a selected cell or synthetic DNA is from a selected cell and the selected cell is further defined as a pathogen, tumor, or bacterial cell.

62. (Amended) The kit of claim 36, wherein the DNA of a selected cell or synthetic DNA is cDNA, fragmented genomic DNA, or synthetic DNA.

III. REQUEST FOR RECONSIDERATION UNDER 37 C.F.R. §1.111

A. Status of the Claims

Claims 34, 36, 37, and 41-65 were pending in the case at the time of the Action. Claims 34, 36, 41-48 and 56-62 were amended herein. Support for the amendments to the claims can be found, at least, in Example 2 at pages 49-52 of the specification. Claims 34, 36, 37, and 41-65 are pending in the case and are presented for reconsideration.

B. Rejection of Claims Under 35 U.S.C. §112, Second Paragraph

The Action rejects claims 34, 36, 37 and 41-65 under 35 U.S.C. §112, second paragraph as allegedly being indefinite for failing to particularly point out the subject matter which Applicant regards as the invention.

(1) The Action rejects claims 34 and 56-65 as not being clear regarding whether claim 34 is drawn to a product or method. Applicants respectfully traverse.

As noted in the Action, the claim is in product-by-process format. The preamble of claim 34 specifies that it is drawn to "Antibodies" and the remainder of the claim specifies the method by which the antibodies are obtained. As such, the claim is in proper product-by-process format and is not indefinite. M.P.E.P §2173.05(p). Removal of the rejection is thus respectfully requested.

(2) The Action rejects claims 57-60 and 62-65 as not containing a sufficient antecedent basis for the limitation "DNA," based on the two recitations of "DNA" in claims 34 and 36.

In response, Applicants note that the rejected claims have been amended, either directly or by dependency upon an amended claim, to correct the antecedent basis. It is believed that the rejection is now moot in light of the amendments. Removal thereof is thus respectfully requested.

C. Rejections Under 35 U.S.C. §112, First Paragraph

Claims 34, 36, and 41-65 stand rejected under the first paragraph of 35 U.S.C. §112 as allegedly lacking an adequate written description of the claimed invention. In particular, the rejection is made with respect to support for the claim limitation "synthetic DNA."

In response, Applicants note that support for the term can be found, at least, at page 41, lines 14-18 of the specification in the following sentences:

> In general, site-directed mutagenesis in accordance herewith is performed by first obtaining a single-stranded vector or melting apart of two strands of a double stranded vector which includes within its sequence a DNA sequence which encodes the desired peptide. An oligonucleotide primer bearing the desired mutated ***sequence is prepared, generally synthetically***. (emphasis added)

As can be seen, the section contemplates synthetically prepared nucleic acids, *e.g.*, synthetic DNA. The claim term thus finds literal support in the specification.

In view of the foregoing, removal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

D. **Rejections Under 35 U.S.C. §102(b)**

The Action rejects claims 34 and 57-58 under 35 U.S.C. §102(b) as anticipated by Pietromonaco *et al.* (PNAS 1990, Vol. 8, pages 1811-1815). In particular, it is stated that the specified process does not confer any distinguishing characteristics on the claimed antibody.

In response, Applicants note that current claim 34 has been clarified as directed to "Antibodies obtained by administering to an animal clones from a sib library of an expression library prepared from DNA of a selected cell or synthetic DNA and collecting antibodies generated in response to an antigen or antigens expressed from said DNA." The prior art does not teach the claimed subject matter, as the recited method for producing antibodies results in a unique population of antibodies. In contrast, Pietromonaco *et al.* is said to teach "*an antibody* obtained by administering to an animal one clone from an expression library from a selected cell type." Emphasis added; Action at page 3.

The claimed antibodies are generated by expression library immunization (ELI). In ELI, a diverse immune response is obtained, based on antigens from known and unknown sequences alike. A unique antibody composition is therefore produced. The technique was not known to those of skill in the art, thus one of skill in the art would have been unable to produce the claimed antibodies. Indeed, at the time the application was filed, the ordinary artisan did not believe that expression library immunization was feasible based on at least the following assumptions in the art: (1) bacterial genes would not sufficiently express in mammalian cells, (2) any expression would be too low to elicit an immune response, (3) ELI would work only in a natural pathogen/host system, (4) interference and/or dominance would prevent the expression of valuable antigens in mixtures, (5) induction of autoimmunity would block protection, and (6) tolerance would be produced by low-level expression of pathogen genes. In further support of

this, attached herewith as **Appendix C** is the Declaration of Dr. Stephen Johnston, which was submitted in parent case serial number 08/421,155.

The prior art therefore does not teach the claimed antibodies "obtained by administering to an animal clones from a sib library of an expression library prepared from DNA of a selected cell or synthetic DNA and collecting antibodies generated in response to an antigen or antigens expressed from said DNA." Unlike the prior art, the approach using the method recited in claim 34 results in the presentation of a diverse set of antigenic determinants, both known and unknown alike. In contrast, the prior art at best teaches generation of an immune response to a small number of known antigens.

In Pietromonaco *et al.*, attempts were made to find antibodies to the "pathogenic epitope" gp330. The procedure used by Pietromonaco *et al.* is predicated upon knowing the identity of the antigenic protein in question (*e.g.*, gp330). By contrast, ELI yields antibodies of known and unknown antigenic protein(s) or epitopes. Further, the procedure used by Pietromonaco *et al.* is an indirect *in vitro* screen. Therefore, antigenic epitopes revealed by this process may have no relevance to an *in vivo* situation. Binding to an antigen *in vitro*, as in a western blot, *etc.*, does not mean that the binding will be "useful" in an *in vivo* situation. For an antibody to be "useful", it must be able to neutralize its cognate antigen, that is, functionally inhibit the activity of said antigen in some way. This functional test is inherent in the process of ELI, since the output of the screen is protection against infection.

The nature of the procedure used by Pietromonaco *et al.* necessitates that it be performed on a protein-by-protein basis, which is labor-intensive and not amenable to high-throughput. Thus, this limits the screening of complex sets of antigens, such as that encoded by a genome, or subset thereof. By contrast, ELI is by its very essence a high-throughput screen, capable of

screening multiple antigens known and unknown antigens simultaneously. A unique collection of antibodies is thus obtained using ELI.

It is finally noted that the term "pathogenic epitopes," as it is used by Pietromonaco *et al.*, is misleading, since it does not use the conventional definition for "pathogenic." This term usually refers to an infectious agent, such as a bacterium, virus or parasite. In this case, the quotation marks indicate that the authors are redefining "pathogenic" to mean disease-causing. That is, "pathogenic" refers to the antigen thought to be responsible for causing the relevant condition studied, the kidney autoimmune disease HN. By contrast, for example, claim 42 defines "pathogen" as a virus, yeast, mold, etc.

In view of the foregoing, removal of the rejection under 35 U.S.C. §102(b) is respectfully requested.

E. Rejections Under 35 U.S.C. §102/§103

(1) The Action rejects claims 34, 41, 42 and 56-60 under 35 U.S.C. §102(b) as allegedly anticipated by or, in the alternative, as being obvious under 35 U.S.C. §103(a) over Fynan (*PNAS* 1993, Vol. 90, pages 11478-11482).

In response, Applicants again note that the cited references do not teach the claimed antibodies. The cited reference is said to teach "*an antibody* against influenza made by genetic immunization." Action at page 4. Again, as indicated above, the method recited in claim 34 results in a unique antibody composition, based on antigens from known and unknown sequences alike. The cited reference does not therefore teach or suggest the composition or the method for creation thereof.

In view of the foregoing, removal of the rejection is respectfully requested.

(2) The Action rejects claims 34, 43, and 56-60 under 35 U.S.C. §102(b) as allegedly anticipated by or, in the alternative, as being obvious under 35 U.S.C. §103(a) over Conry (*Cancer Research*, 1994, Vol. 54, pages 1164-1168).

In response, Applicants once again note, for the reasons cited above, that the cited reference does not teach the claimed antibodies. As indicated above, the method recited in claim 34 results in a unique antibody composition. The method by which the antibody composition is made was neither known nor obvious to those of skill in the art at the time the invention was made. As such, the cited reference does not render the claims obvious.

In view of the foregoing, removal of the rejection is respectfully requested.

(3) The Action rejects claims 34, 36, 37, 41, 44-50, 52-55, 56 and 61-65 under 35 U.S.C. §102(b) as allegedly anticipated by or, in the alternative, as being obvious under 35 U.S.C. §103(a) over Butman (U.S. Patent No. 4,950,589).

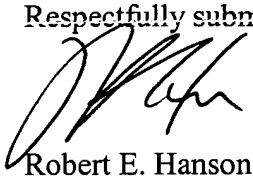
In response, Applicants once again note that the cited reference does not teach the claimed antibodies. As indicated above, the method recited in claim 34 results in a unique antibody composition. The method by which the antibody composition is made was neither known nor obvious to those of skill in the art at the time the invention was made.

In view of the foregoing, removal of the rejection is respectfully requested.

F. Conclusion

In light of the foregoing, applicants submit that all claims are in condition for allowance, and an early indication to that effect is earnestly solicited. The examiner is invited to contact the undersigned (512)536-3085 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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Date: February 3, 2003

APPENDIX A: MARKED UP COPY OF CLAIM AMENDMENTS

34. (Three Times Amended) [An antibody] Antibodies obtained by administering to an animal [one or more] clones from a sib library of an expression library prepared from DNA of a selected cell or synthetic DNA and collecting [at least one antibody] antibodies generated in response to an antigen or antigens expressed from said DNA.

36. (Three Times Amended) An immunodetection kit for detecting a pathogen, comprising:

(a) [an antibody or] antibodies prepared by administering to an animal [one or more] clones from a sib library of an expression library prepared from DNA of a selected cell or synthetic DNA and collecting [at least one antibody] antibodies generated in response to an antigen or antigens expressed from said DNA;

(b) a suitably aliquoted composition of the pathogen; and

(c) an immunodetection means.

41. (Twice Amended) The antibodies[y] of claim 56, wherein the selected cell is a pathogen cell.

42. (Amended) The antibodies[y] of claim 41, wherein the pathogen is a virus, yeast, mold, yeast, algae or protozoa.

43. (Twice Amended) The antibodies[y] of claim 56, wherein the selected cell is a tumor cell.

44. (Twice Amended) The antibodies[y] of claim 56, wherein the selected cell is a bacterial cell.

45. (Amended) The antibodies[y] of claim 44, wherein the bacterial cell is a *Mycoplasma pulmonis, Mycobacterium tuberculosis* or *Listeria monocytogenes* cell.

46. (Amended) The antibodies[y] of claim 44, wherein the bacterial cell is a *Mycoplasma pulmonis* cell.

47. (Amended) The antibodies[y] of claim 44, wherein the bacterial cell is a *Mycobacterium tuberculosis* cell.

48. (Amended) The antibodies[y] of claim 44, wherein the bacterial cell is a *Listeria monocytogenes* cell.

56. (Amended) The antibodies[y] of claim 34, wherein the DNA is from a selected cell and the selected cell is further defined as a pathogen, tumor, or bacterial cell.

57. (Amended) The antibodies[y] of claim 34, wherein the DNA of a selected cell or synthetic DNA is cDNA, fragmented genomic DNA, or synthetic DNA.

58. (Amended) The antibodies[y] of claim 57, wherein the DNA is cDNA.

59. (Amended) The antibodies[y] of claim 57, wherein the DNA is fragmented genomic DNA.

60. (Amended) The antibodies[y] of claim 57, wherein the DNA is synthetic DNA.

61. (Amended) The kit of claim 36, wherein the DNA of a selected cell or synthetic DNA is from a selected cell and the selected cell is further defined as a pathogen, tumor, or bacterial cell.

62. (Amended) The kit of claim 36, wherein the DNA of a selected cell or synthetic DNA is cDNA, fragmented genomic DNA, or synthetic DNA.